UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/796,062	03/10/2004	Minoru Yamaguchi	OKA-0216	2613

23353 7590 05/02/2007

RADER FISHMAN & GRAUER PLLC
LION BUILDING
1233 20TH STREET N.W., SUITE 501
WASHINGTON, DC 20036

EXAMINER
HINES, JANA A

ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
05/02/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/796,062	YAMAGUCHI ET AL.	
	Examiner	Art Unit	
	Ja-Na Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/10/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

1. Claims 1-11 are under consideration in this office action.

Information Disclosure Statement

2. The information disclosure statement (IDS) submitted on March 10, 2004 was entered. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Specification

3. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code at page 2, line 6. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

4. Page 13, Line 21 recites "N-ciotinylcysteic acid" instead of "N-biotinylcysteic acid." Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicant(s) regard as their invention.

a) The preamble of the claims is drawn to a method for determining amino acid sequence of a peptide, comprising a preparation step; a coupling step; and a subjecting step. There is no correlation step which correlates determining the amino acid sequence and subjecting the coupled product to mass spectrometry analysis. Therefore, the goal of the preamble is not commensurate with the steps of the method that are drawn to determining the amino acid sequence.

b) Claim 1 recites the phrase "amino acid derivatives" however it is unclear how to define "derivatives". The derivative language is vague and indefinite because the characteristics needed to determine whether an unknown could be considered a derivative of an amino acid are unknown. The specification does it teach a requisite amount of retained qualities needed or characteristics necessary to determine amino acid derivatives. Therefore the claims are unclear.

c) Claim 8 recites the limitation "the C-terminal side of a basic amino acid residue" in the claim. There is no basic amino acid residue recited in claim 1. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-3 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Bauer et al., (2000. Rapid Comm. In Mass Spectrometry. Volume 14, Issue 10, Pages 924-929).

Claim 1-4 and 8-11 are drawn to a method for determining amino acid sequence of a peptide, comprising the steps of: preparing a peptide of interest or fragments thereof obtained by optionally cleaving the peptide of interest; coupling an amino acid derivative to the N-terminus of the peptide of interest or the fragments thereof, the amino acid derivative having protected an amino group with a protective group and derived from an amino acid with a side chain containing an acidic group; and subjecting the coupled product to mass spectrometry analysis. Claim 2 is drawn to the acidic group; claim 3 is drawn to the amino acid; claim 8 is drawn to the hydrolysis of the C-terminal side; claim 4 are drawn to the protective group; claim 9 is drawn to the ionization and decay of the peptide; claim 10 is drawn to the ionization by ionized by matrix-assisted laser desorption ionization (MALDI); and claim 11 is drawn to separation and detection by time-of-flight mass spectrometry (TOFMS).

Bauer et al., teach a method for determining amino acid sequence of a peptide, comprising: preparing a peptide of interest by cleaving the peptide of interest; coupling an amino acid derivative to the N-terminus of the peptide of interest, wherein the amino acid derivative having protected an amino group with a protective group and derived from an amino acid with a side chain containing an acidic group; and subjecting the coupled product to mass spectrometry analysis (abstract). Bauer et al., teach the model peptide was oxidized with performic acid to convert the cysteine to cysteic acid, was

analyzed by mass spectrometry (page 925, col.1). Bauer et al., teach the sulfonic acid derivatization of the N-terminus using chlorosulfonylacetyl chloride and performic acid oxidation of cysteine were carried out (page 925, col. 1). Thereby Bauer et al., teach coupling the amino acid derivative to the peptide of interest. Bauer et al., teach the N-terminal acid group being generated by converting the side chain of the cysteine to cysteic acid by exposure to performic acid (page 926, col. 1). The acidic group of cysteic acid is a sulfo group and the amino acid is cysteic acid. The use of highly acidic, N-terminal derivatives simplifies the interpretation of fragment ion spectra for peptide ions produced by ionization techniques (page 924, col. 2). Bauer et al., teach derivatization techniques has improved the quality of PSD-MADLI spectra (page 924, col.2).

Bauer et al., teach subjecting the derivatized product to mass spectrometry were the mass specta provided peptide sequence interpretation (page 925, col.2). Mass spectrometry has become a standard approach for the identification and characterization of proteins (page 924, 926 col.1 and 2). Bauer et al., teach preparing a peptide of interest obtained by cleaving the peptide of interest wherein the derivatization procedure depends on derivatized tryptic digests of proteins (page 927, col.2). Bauer et al., teach sequence information is provided when techniques involve using a protease (page 924, col.1). Tryptic digests have the advantage of producing peptides possessing a basic residue at their C-terminus (page 924, col. 1). Therefore, Bauer et al., teach cleavage performed by the trypsin enzyme that specifically hydrolyzes a peptide bond on the C-terminal side of a basic amino acid residue.

Bauer et al., teach claims 1-4 and 8-11 of the instant application.

7. Claims 1-4 and 9-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Keough et al., (1999. PNAS Vol. 96:7131-7136).

Claim 1 is drawn to a method for determining amino acid sequence of a peptide, comprising the steps of: preparing a peptide of interest or fragments thereof obtained by optionally cleaving the peptide of interest; coupling an amino acid derivative to the N-terminus of the peptide of interest or the fragments thereof, the amino acid derivative having protected an amino group with a protective group and derived from an amino acid with a side chain containing an acidic group; and subjecting the coupled product to mass spectrometry analysis. Claim 2 is drawn to the acidic group; claim 3 is drawn to the amino acid; claim 4 are drawn to the protective group; 9 is drawn to the ionization and decay of the peptide; claim 10 is drawn to the ionization by ionized by matrix-assisted laser desorption ionization (MALDI); and claim 11 is drawn to separation and detection by time-of-flight mass spectrometry (TOFMS).

Keough et al., teach a method for determining amino acid sequence of a peptide, comprising the steps of: preparing a peptide of interest obtained by cleaving the peptide of interest; coupling an amino acid derivative to the N-terminus of the peptide of interest wherein the amino acid derivative has a protected amino group with a protective group and derived from an amino acid with a side chain containing an acidic group; and subjecting the coupled product to mass spectrometry analysis (page 7132). Keough et al., teach a method involves the addition of a strong acid group (amino acid derivative)

Keough et al., teach considerable enhancement of the N-terminal ion after enhancement which aided in the complete sequencing of the peptide (page 7133, col.1). Keough et al., teach procedures for high-sensitivity tryptic peptide sequencing using Matrix-Assisted Laser Desorption Ionization Spectrometry Post Source Decay (PSD MALDI) and routes to produce tryptic peptides containing an N-terminal sulfonic acid. The peptide of interest has been cleaved with a tryptic enzyme before coupling the N-terminus of the peptide.

Keough et al., teach the N-terminal derivatization procedures involve coupling an amino acid derivative to the N terminus of peptides (page 7132, col.1). This derivatization reaction introduces an aromatic sulfonic acid group directly at the N terminus of the peptide (page 7133, col.2). Keough et al., also teach peptides derivatized with carboxylic acids (page 7132, col.1). Therefore Keough et al., teach a derivative derived from an amino acid with a side chain containing an acidic group such as a sulfo group found on cysteic acid. Keough et al., teach the PSD MALDI analysis of a commercially available peptide, CDPGYIGSR (page 7133, col.1). Keough et al., also teach analysis with Time-of-Flight mass (TOF) spectrometry (page 7131, col.1). Keough et al., shows in the lower drawing of Fig. 1, an improved spectrum after oxidation of the N-terminal cysteine to cysteic acid and the complete sequence of the peptide could be determined by PSD MALDI after oxidation (page 7133, col. 1). Keough et al., teach that PSD MALDI mass spectrometry was developed for high-sensitivity peptide sequencing applications has become an increasingly essential tool for protein and peptide

sequencing because of its speed, sensitivity, and applicability to analyze complex mixtures (page 7131, col.1).

Keough et al., teach claims 1-4 and 9-11 of the instant application.

8. Claims 1 and 9-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Nakanishi et al., Publication Number 2001-235477, (published August 31, 2001).

Claim 1 is drawn to a method for determining amino acid sequence of a peptide, comprising the steps of: preparing a peptide of interest obtained by coupling an amino acid derivative to the N-terminus of the peptide of interest, the amino acid derivative having protected an amino group with a protective group and derived from an amino acid with a side chain containing an acidic group; and subjecting the coupled product to mass spectrometry analysis. Claim 9 is drawn to the ionization and decay of the peptide; claim 10 is drawn to the ionization by ionized by matrix-assisted laser desorption ionization (MALDI); and claim 11 is drawn to separation and detection by time-of-flight mass spectrometry (TOFMS).

Nakanishi et al., teach coupling an amino acid derivative to the N-terminus of the peptide of interest, the amino acid derivative having protected an amino group with a protective group and derived from an amino acid with a side chain containing an acidic group; and subjecting the coupled product to mass spectrometry analysis (para. 0014). Nakanishi et al., adds a specific fluorescent material to a peptide and analyzing the Matrix-Assisted Laser Desorption Ionization Time of Flight Mass Spectrometry Post Source Decay (MALDI-TOF-MAS-PSD) (para. 0006). Nakanishi et al., teach that the

mass spectrometric methods are not limited to the fluorescent labeling reagent of the peptide (para. 0011). Nakanishi et al., teach combining or coupling the N-terminal cysteine in a peptide with the fluorescein compound (para. 0014). Nakanishi et al., teach if not cysteine is present, then a cysteine is added to the amino terminal side of the peptide when the amino terminal of the peptide is not a cysteine (para. 0014). An analysis by mass spectrometry of the labeled peptide derivative is performed using the PSD technique of MALDI-TOF (para. 0016). Nakanishi et al., the method of determining an amino acid sequence by using the amino terminal of the peptide to aid in chemically induced detection (para. 0004). Nakanishi et al., teach the ionization and decay of the peptide; ionized by MALDI; and detection by time-of-flight mass spectrometry (TOFMS) (para. 0016).

Nakanishi et al., teach claims 1 and 9-11 of the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Turecek (2002. J. Mass Spectrometry. Vol. 37:1-14) in view of Keough et al., (1999. PNAS Vol. 96:7131-7136).

Claim 1 is drawn to a method for determining amino acid sequence of a peptide, comprising the steps of: preparing a peptide of interest or fragments thereof obtained by optionally cleaving the peptide of interest; coupling an amino acid derivative to the N-terminus of the peptide of interest or the fragments thereof, the amino acid derivative having protected an amino group with a protective group and derived from an amino acid with a side chain containing an acidic group; and subjecting the coupled product to mass spectrometry analysis. Claim 2 is drawn to the acidic group; claim 3 is drawn to the amino acid; claims 4-6 are drawn to the protective group; claim 7 is drawn to a N-biotinylcysteic acid; claim 10 is drawn to the ionization by ionized by matrix-assisted laser desorption ionization (MALDI); and claim 11 is drawn to separation and detection by time-of-flight mass spectrometry (TOFMS).

Turecek teach a method for determining amino acid sequence of a peptide, comprising preparing a peptide of interest obtained by cleaving the peptide of interest; coupling an amino acid derivative to the N-terminus of the peptide of interest, the amino acid derivative having protected an amino group with a protective group and subjecting the coupled product to mass spectrometry analysis (see Figure 6 and Schemes 6 and 8). The Isotope-Coded Affinity Tags for protein (ICAT) analysis, wherein ICAT relies on *in vitro* derivatization with biotinylated tags on proteins, followed by matrix-assisted laser desorption ionization (MALDI) (page 8, col.2). Turecek teach peptide sequencing (page 10, col.1). Turecek teaches that derivatization ensures selective conjugation of the N-terminal cysteine or at N-terminal serine or theronine groups (page 8,col. 2). Turecek

also teach of cysteine-targeting affinity tags wherein following tryptic digestion, the biotin derivatives couple with cysteine (page 11, col.2).

Turecek teach the N-terminal biontylated proteins whose serine and theronine residues were targeted, followed by digestion and MALDI-TOFMS analysis (page 11-12, col.2-1). Turecek teaches that cysteines are derivatized with the biotin tag via the thiol specific reactive group (Figure 6). Turecek teach the advantage of using the biotinylated cysteine tag to provide stronger yet reversible links (page 9, col.1). This selective affinity method simplifies the peptide mixture and does not interference with the mass spectrometric MALDI-TOFMS analysis (page 9, col.2). Turecek teach that common proteolytic enzymes such as trypsin does not interfere with the biotin label (page 9, col1). However Turecek does not teach the amino acid derivative being from an amino acid with a side chain containing an acidic group.

Keough et al., teach a method involves the addition of an amino acid derivative having a strong acid group (amino acid derivative) to the N terminus of tryptic peptides before MALDI analyses (page 7132, col.1). The N-terminal derivatization procedures involve coupling an amino acid derivative to the N terminus of peptides (page 7132, col.1). This reaction introduces an aromatic sulfonic acid group directly at the N terminus of the peptide (page 7133, col.2). Keough et al., teach MALDI procedures for high-sensitivity tryptic peptide sequencing to produce tryptic peptides containing an N-terminal sulfonic acid (page 7132, col.1). Therefore Keough et al., teach a derivative derived from an amino acid with a side chain containing an acidic group such as a sulfo group found on cysteic acid (page 7132, col.1). Keough et al., show an improved

spectrum after oxidation of the N-terminal cysteine to cysteic acid (page 7133, col. 1). Keough et al., teach considerable enhancement of the N-terminal ion after enhancement which aided in the complete sequencing of the peptide (page 7133, col.1).

Therefore it would have been prima facie obvious at the time of applicants invention to add of an amino acid derivative having a strong acid group to Turecek's method for determining amino acid sequence of a peptide, comprising preparing a peptide of interest obtained by cleaving the peptide of interest; coupling an amino acid derivative to the N-terminus of the peptide of interest, the amino acid derivative having protected an amino group with a protective group and subjecting the coupled product to mass spectrometry analysis in order to provide an improved mass spectrometric spectrum after oxidation to a cysteic acid. One of ordinary skill in the art would have a reasonable expectation of success modifying the method of determination as taught by Turecek because Turecek already teach that derivatization ensures selective conjugation of the N-terminal cysteine while protecting the amino group and Keough teach considerable enhancement within the mass spectra result. Furthermore, no more than routine skill would have been required to use an amino acid derivative with a side chain having an acidic group since Keough et al., this technique is well known to aide in the complete sequencing of the peptide using MALDI-TOF analysis.

Conclusion

10. No claims allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Jeffery Siew, can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ja-Na Hines
April 25, 2007

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER